Chow RT, Johnson MI, et al. Efficacy of low-level laser therapy [LLLT] in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. Lancet 2009;374:1897-1908.

Design: Meta-analysis of randomized clinical trials

PICOS:

- **Patients:** acute or chronic neck pain as defined by trial investigators; exclusions were of patients with specific pathological changes (arthritis, fibromyalgia, radiculopathy, neurological disease)
- **Interventions:** Laser device that delivered irradiation to point in the neck identified by tenderness, local acupuncture points, or on a grid at predetermined points overlying the neck
- **Comparison:** placebo laser with an identical laser device in which the laser emission was deactivated, or an active treatment control (e.g., exercise)
- **Outcome:** pain relief on a 0-100 mm scale, or patient-reported improvement (categorical reports of no relief, complete relief, etc); functional improvements were acceptable as secondary measures of effect
- **Study types:** randomized or quasi-randomized trials

Study search and selection:

- Databases included MEDLINE, EMBASE, CINAHL, the Physiotherapy Evidence Database, and the Cochrane Central Register
- Non-English studies were translated by one of the authors
- Two reviewers independently read the studies and extracted data, with disagreements resolved through discussion with other team members
- The Jadad scale was used for quality assessment, which awards points for randomization, double-blinding, and description of dropouts; there is a maximum score of 5 points, and studies with 3 or more points were considered high quality

Results:

- 16 randomized clinical trials with 820 patients were suitable for inclusion
- 2 studies were of acute neck pain; 14 were for chronic pain
- 5 of the chronic pain studies reported categorical data for improvement; the pooled relative risk of improvement (relative benefit) was 4.05 (95% CI, 2.74 to 5.98) in favor of low level laser, with low heterogeneity
- 11 trials reported mean differences of pain scores on a 0-100 mm scale; the weighted mean difference in favor of low level laser at the end of treatment was 19.65 points (95% CI, 10.04 to 29.68), with considerable heterogeneity
    - Two studies reported two different levels of laser intensity, and were reported separately
- 4 studies with 171 patients reported mean pain score differences at follow-up 1-4 weeks after treatment; the weighted mean difference in favor of low level laser was 20.46 points (95% CI, 13.6 to 27.33)

    - At 22 weeks, the difference in favor of laser was 23.44 points (95% CI, 17.11 to 29.7)
- Disability scores were pooled in 5 studies with 314 patients; the standardized mean difference in favor of laser was 1.38 SD (95% CI, 0.39 to 2.37)
    - A SMD of 0.8 SD or greater is generally considered large

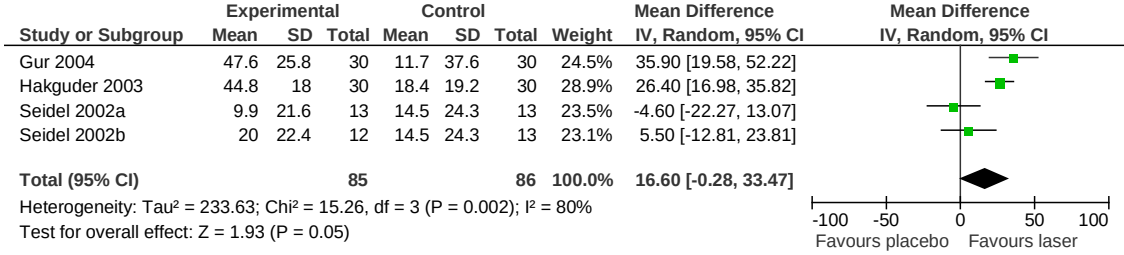
Authors' conclusions:

- LLLT shows moderate statistical evidence for efficacy in the short and medium term for acute and chronic neck pain
- The average reduction of 19.86 mm on pain VAS is clinically important
- Heterogeneity in the meta-analyses was reduced when variations in doses and application procedures were accounted for
- Although many apparently disparate diagnostic terms are applied to patients with neck pain, a definitive diagnosis of the cause of neck pain is not possible in a clinical setting, and the term "non-specific neck pain" encompasses many descriptors
- There is little reason to believe that factors other than a plausible anatomic target, dose per point, and irradiation times are essential for the efficacy of class 3B lasers (5 mW -500 mW)
- The optimum dose for wavelength 820-830 nm was 5.9 joules with an irradiation time of 39.8 sec; and for 904 nm, 2.2 joules with an irradiation time of 238 sec

Comments:

- The Jadad scale was used for quality of included studies
- This is a 5 point scale which awards one point each for a study being described as randomized and double blind, and one point for accounting for dropouts; the description of randomization and blinding may add or subtract points
- Since 3 points was sufficient to qualify a study as high quality, it is not clear that certain factors were considered in judging whether a study had a high risk of bias, or was even very informative
    - Concealment of allocation, display of baseline data for both groups, well-described inclusion/exclusion criteria, and chronicity of pain were not considered in pooling the various trials
- Sponsorship is not reported in most of the original studies; Ceccherelli 1989 had an acknowledgement for the device manufacturer; and, since none of the studies was done in the USA, protocols and trial registration cannot be examined, and bias is a real possibility
- In addition to the issues with bias in the included studies, the method of pooling studies is dubious in some instances
    - In Figure 5, the follow-up pain reduction is pooled with a fixed-effect model, in spite of heterogeneity which would generally require a random-effects model
    - The fixed-effect model for follow-up of 1-4 weeks shows a pooled effect of 20.46 points with confidence intervals from 13.60 to 27.33

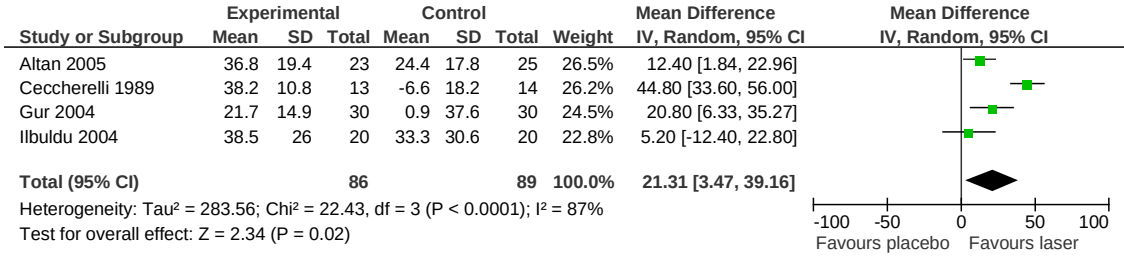
- The more appropriate random-effects model shows a pooled effect of 16.6 points with CI from -0.28 to 33.47 (losing statistical significance)



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Gur 2004	47.6	25.8	30	11.7	37.6	30	24.5%	35.90 [19.58, 52.22]
Hakguder 2003	44.8	18	30	18.4	19.2	30	28.9%	26.40 [16.98, 35.82]
Seidel 2002a	9.9	21.6	13	14.5	24.3	13	23.5%	-4.60 [-22.27, 13.07]
Seidel 2002b	20	22.4	12	14.5	24.3	13	23.1%	5.50 [-12.81, 23.81]
Total (95% CI)			**85**			**86**	**100.0%**	**16.60 [-0.28, 33.47]**

Heterogeneity: Tau² = 233.63; Chi² = 15.26, df = 3 (P = 0.002); I² = 80%
Test for overall effect: Z = 1.93 (P = 0.05)

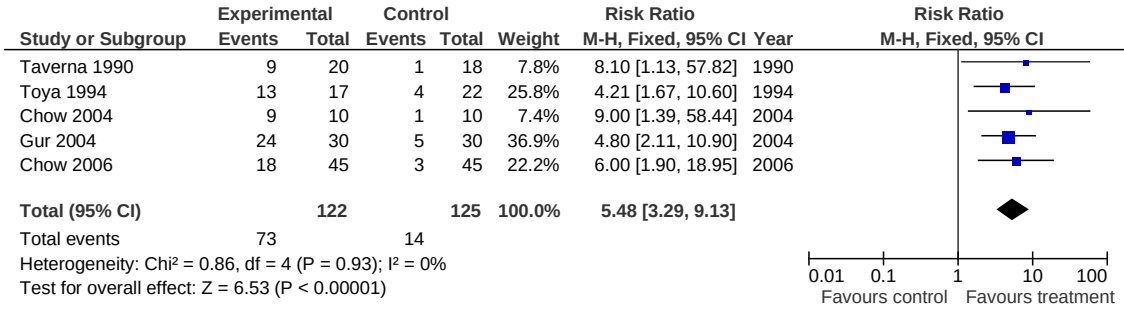
- Similarly, the follow-up 10-22 weeks random effects model, though similar in overall size to that in the second part of Figure 5 (23.44 points, CI from 17.11 to 29.77), has considerably wider confidence intervals from 3.47 to 39.16



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Altan 2005	36.8	19.4	23	24.4	17.8	25	26.5%	12.40 [1.84, 22.96]
Ceccherelli 1989	38.2	10.8	13	-6.6	18.2	14	26.2%	44.80 [33.60, 56.00]
Gur 2004	21.7	14.9	30	0.9	37.6	30	24.5%	20.80 [6.33, 35.27]
Ilbuldu 2004	38.5	26	20	33.3	30.6	20	22.8%	5.20 [-12.40, 22.80]
Total (95% CI)			**86**			**89**	**100.0%**	**21.31 [3.47, 39.16]**

Heterogeneity: Tau² = 283.56; Chi² = 22.43, df = 3 (P < 0.0001); I² = 87%
Test for overall effect: Z = 2.34 (P = 0.02)

- In several of the included trials, the description of randomization is vague, and allocation concealment cannot be assumed; terms such as “randomly subdivided,” “simple systematic manner (x+1)” are not clear
- Figure 4, which pools the weighted mean differences of pain reduction from baseline to post-treatment, includes at least one study (Chow 2006) in which the groups were unbalanced at baseline, so that some of the pain reduction in the laser group could have arisen from regression to the mean and other artifacts
- However, these problems do not necessarily compromise the overall conclusions regarding LLLT, specifically with respect to Figure 3, the relative risk of global improvement
    - Using data from Gur 2004, Chow 2004, and Chow 2006, it is possible to define “global improvement” as 50% improvement (Gur and Chow 2004), or as “much improvement” (Chow 2006)
    - The relative risk of global improvement is greater in favor of LLLT if this analysis is done for Figure 3; the RR is 5.48 instead of 4.05 (Taverna and Toya are unavailable, but removing them increases the RR to 5.67):



- The standardized mean differences for disability in Figure 6 show a very large pooled effect size of 1.38 standard deviations in favor of laser, but in three of the studies, concealment of allocation was poorly described (clear in Chow 2006, and probably satisfactory in Gur 2004); re-analysis of the disability data with only Chow and Gur leaves a pooled difference of 0.84 SD, which is still considered fairly large
- It is not clear that the heterogeneity mainly arises from dose and irradiation times, or that the nature of the neck pain is not a factor
    - One study with a very small effect size (Dundar 2006) did not clearly exclude patients with radicular cervical symptoms; other studies with large effect sizes (Ozdemir 2001, Ceccherelli 1989, Chow 2004, Gur 2004, Chow 2006) did explicitly exclude patients with signs of cervical radicular syndromes
- Therefore, patient selection, and not just dose and irradiation time, may account for some heterogeneity in the data
- Dosage and appropriate frequency remain difficult to define, due to variations in the details of administration
- The congruity of the intervention with general guideline values (e.g., being a passive modality with unclear methods of delivery) is not clear from the literature alone, and must be discussed with the guideline task force

Assessment: Adequate for good evidence that LLLT may reduce pain and improve function in patients with neck pain and no radicular involvement; however, the consistency of the intervention with general guideline values is not clear and requires separate consideration